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Cardiac lymphatics – a new target for prevention of heart failure?

Dr Ebba Brakenhielm

INSERM U1096,

Normandy University & University of Rouen

Institute for Research and Innovation in Biomedicine, Rouen, France

Recent years have seen an important advance in our understanding of the molecular regulation and pathophysiological importance of lymphangiogenesis1: while it is now accepted that tumor and lymph node lymphangiogenesis contribute to the metastatic spread of many solid tumor types, insufficient lymphangiogenesis occurs in various diseases characterized by chronic swelling and/or inflammation, including lymphedema, psoriasis, arthritis, and irritable bowel syndrome, but also in atherosclerosis. In this talk, I will present the state-of-the art concerning lymphatic function and lymphangiogenesis in the heart in health and disease. Indeed, recent experimental studies have revealed that insufficient cardiac lymphangiogenesis contributes to deleterious cardiac remodeling after myocardial infarction2,3. The molecular links between lymphatic transport deficiencies and chronic edema, inflammation and fibrosis will be discussed in relation to ischemic or non-ischemic heart disease, and current strategies to improve lymphatic transport will be presented.

References

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3 Henri, O. *et al.* Selective Stimulation of Cardiac Lymphangiogenesis Reduces Myocardial Edema and Fibrosis Leading to Improved Cardiac Function Following Myocardial Infarction. *Circulation* **133**, 1484-1497; discussion 1497, (2016).

Short biography

Dr Ebba Brakenhielm

Dr Ebba Brakenhielm, initially trained at Stockholm University in Sweden as chemist, specializing in neurochemistry and cellpenetrating peptides for delivery of therapeutic molecules, performed her PhD studies (1999-2003) in tumor biology at the Karolinska Institutet in the laboratory of Pr Yihai Cao. The thematic of her research work was "Discovery and Characterization of Novel Angiogenesis Inhibitors in pathophysiology", including evaluations of anti-angiogenic treatments in the setting of tumor growth but also in adipose tissue expansion in obesity. She also participated in studies of therapeutic angiogenesis for ischemic diseases. Her postdoctoral training (2004-2005) was at UCLA, California, in the laboratory of Pr. Lily Wu, focusing on molecular imaging to unravel the links between tumor lymphangiogenesis and distal metastasis in prostate and breast cancer xenograft models.

Since 2006 she is a tenured researcher (CR1 Inserm) in a cardiovascular research laboratory, "Endothelium, Valvulopathy, and Heart Failure" Inserm UMR1096 (directed by Pr Vincent Richard), at the Normandy University (UNIRouen) in France, where she currently directs a team composed of one junior scientist, 3 graduate students, and technical personnel (1 research engineer and 2 technicians). Together with collaborators in France and abroad, she has been investigating the impact of therapeutic stimulation of blood and lymphatic vessel growth in cardiovascular diseases, in particular in heart failure. Since 2017, Ebba is coordinating an ERA-CVD grant "LYMIT-DIS" working together with Dr Anna Ratajska (Warsaw Medical School), and others to decipher the role of lymphatics in HFpEF. https://lymit-dis.eu/

Recent research contributions:

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4. Brakenhielm E, Burton JB, Johnson M, Charvarria N, Morizono K, Chen I, Alitalo K, and Wu L Modulating metastasis by a lymphangiogenic switch in prostate cancer. Int J Can 2007 121(10):2153-2161 (cited 36 times) IF:4.7

5. Nissen LJ, Cao R, Hedlund EM, Wang Z, Zhao X, Wetterskog D, Funa K, Brakenhielm E, and Cao Y Angiogenic factors FGF2 and PDGF-BB synergistically promote murine tumor neovascularization and metastasis. J. Clin. Invest. 2007 117(10):2766–2777 (cited 188 times) IF:16.6